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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/798,721	03/11/2004	D. Wade Walke	LEX-0477-USA	5023

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EXAMINER	
LI, RUIXIANG	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 10/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/798,721	WALKE ET AL.	
	Examiner	Art Unit	
	Ruixiang Li	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7 and 8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 7, and 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

Applicants' response filed on 08/17/2005 has been entered in full. Claims 1, 7, and 9 are pending and under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Withdrawn Objections and/or Rejections

The rejection of claims 1, 7, and 8 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4, and 6 of U.S. Patent No. 6,777,232 has been withdrawn in view of submitted terminal disclaimer on 08/17/2005.

Claim Rejections under 35 USC § 112, 1st paragraph, Scope of Enablement

The rejection of claims 1, 7, and 8 under 35 U.S.C. 112, first paragraph for scope of enablement is maintained.

Beginning at page 2 of Applicants' response filed on 08/17/2005, Applicants criticize Examiner's position and argue that there is absolutely no requirement that all species of an invention must have all of the exactly same properties, or specifically, that novel

nucleotide fragments of SEQ ID NO: 9 must have the exact same function as the full length sequence of SEQ ID NO: 9. Applicants submit, citing case law, that it is well established that the enablement requirement is met if any use of the invention (or in this case, certain species of the invention) is provided.

Applicants' argument has been fully considered, but is not deemed to be persuasive for the following reasons. Claim recites a genus of nucleic acid molecules of any size comprising at least 80 contiguous nucleotides of SEQ ID NO: 9, not fragments of SEQ ID NO: 9. While some of species of the genus may retain a readily apparent use of the full-length molecule, the instant disclosure would not be found to be enabling for the whole genus because (i) there is no evidence that 80 residues are sufficient to retain the functions of the full length and (ii) even if so, there is no guidance regarding which 80 residues are sufficient.

While there is no requirement for all species of a genus to have exactly same properties, the disclosure has to reasonably enable an artisan to make and use the genus. Applicants' argument that the enablement requirement is met if any use of the invention (or in this case, certain species of the invention) is provided is incorrect. To satisfy the enablement requirement, the disclosure must teach how to make and use the invention. Merely providing asserted uses does not satisfy the enablement requirement under 35 U.S.C. §112, first paragraph. In the instant case, the disclosure must provide sufficient guidance and/or working examples to guide an artisan to make and use the

genus, not just the full length nucleic acid sequence of SEQ ID NO: 9, which encodes an amino acid sequence of SEQ ID NO: 10.

If Applicants intend to claim for a genus of nucleic acid molecules as being used for primers or probes, the instant disclosure fails to provide information or sufficient guidance on how to make and use the claimed genus. One skilled in the art may be able to use, for example, a nucleic acid molecule consisting of at least 80 contiguous nucleotide of SEQ ID NO: 9. However, one skilled in the art would not be able to use the claimed broad genus to specifically determine, for example, the expression of the instantly claimed nucleic acid in a tissue, due to the unpredictable nature of nucleic acid hybridisation and the possibility that a claimed nucleic acid molecule may hybridize to a nucleic acid other than the portion of SEQ ID NO: 9. The state of the art is such that determining the specificity of hybridization is empirical by nature and the effect of mismatches is unpredictable, as taught by Wallace et al. (Methods Enzymol. 152:432-443, 1987) and Sambrook et al. (Molecular Cloning, A Laboratory Manual, 2nd Edition, 1989, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, page 11.47).

At the middle of page 3 of Applicants' response filed on 08/17/2005, Applicants argue that the action focuses on a single aspect of the present invention. This is not found to be persuasive because the scope enablement issue is judged in the action against the well-established Wands factors, as recited in the office action.

Beginning at the middle of page 3 of Applicants' response filed on 08/17/2005, Applicants argue that, with respect to the quantity of experimentation necessary, significant commercial exploitation of the presently claimed sequences requires no more information than the nucleic acid sequence itself. Applicants submit that as the nucleic acid sequence of SEQ ID NO: 9 is clearly disclosed in the specification, such commercial exploitation requires no experimentation.

Applicants' arguments have been fully considered but are not deemed to be persuasive because the present invention is not limited to the sequence of SEQ ID NO: 9. Rather, claim 1 encompasses a genus of nucleic acid comprising at least 80 contiguous bases of nucleotide sequence from SEQ ID NO: 9. The specification, while enabling a single nucleic acid sequence of SEQ ID NO: 9, does not provide sufficient guidance and/or working examples to make and use the genus of claimed nucleic acids. In order to practice the present invention, one of skill in the art would have to first determine the structure and biological function of the nucleic acids encompassed by the instant claims. Accordingly, to make and use the genus of claimed nucleic acid requires undue experimentation.

Beginning at the middle of page 4 of Applicants' response filed on 08/17/2005, Applicants argue, with regard to the amount of direction or guidance presented, that there is sufficient knowledge and technical skill in the art for a skilled artisan to be able to make and use the claimed DNA species in a number of different aspects of the invention entirely without further details in a patent specification.

Applicants' argument has been fully considered but is not deemed to be persuasive because while standard molecular biological techniques are routine in the art, the general teachings in the art are not directed to the specific genus of the nucleic acids of the present invention and do not provide sufficient guidance on how to make and use the claimed genus of nucleic acid molecules. One skilled in the art may be able to use, for example, a nucleic acid molecule consisting of at least 80 contiguous nucleotide of SEQ ID NO: 9 as primers or probes in PCR based screening and determining tissue expression patterns. However, an artisan would not be able to use the claimed broad genus to specifically determine, for example, the expression of the claimed nucleic acid in a tissue, due to the unpredictable nature of nucleic acid hybridisation and the possibility that a claimed nucleic acid molecule may hybridize to a nucleic acid other than the portion of SEQ ID NO: 9. Thus, neither the specification nor the art provides sufficient guidance on how to make and use the present invention.

At the middle of page 5 of Applicants' response filed on 08/17/2005, Applicants acknowledge, with regard to the existence of working examples, that thee are no

working examples in the specification.

Beginning at the bottom of page 5 of Applicants' response filed on 08/17/2005, Applicants argue that, with regard to the predictability or unpredictability of the art, the predictability of the art is quite high with regard to a large number of different applications utilizing the claimed nucleic acid sequences. Applicants question the relevance of the publication of Ngo et al., which was published in1994, and submit that the argument is misplaced.

Applicants' argument has been fully considered but is not deemed to be persuasive because given a specific nucleic acid sequence, such as the sequence of SEQ ID NO: 9, the predictability of the art is high with regard to applications such as gene expression analysis or profiling. However, claim 1 is not only drawn to SEQ ID NO: 9, rather a genus of nucleic acids. Since the structure and biological activity of the nucleic acids encompassed by the instant claim are unknown, it is, consequently, unpredictable regarding their applications such as gene expression analysis or profiling.

At the middle of page 6 of Applicants' response filed on 08/17/2005, Applicants argue that, with regard to the breadth of the claims, all of the species encompassed in the present claims can be utilized in most, if not all, of the applications, including gene expression analysis or profiling, chromosomal mapping and genomic cloning, PCR, recombinant expression. Applicants submit that although somewhat broad, the

presently claimed invention clearly meets the enablement requirement under eighth "Wands factors".

Applicants' argument has been fully considered but is not deemed to be persuasive because claim 1 recites a genus of nucleic acid molecules of any size that has at least 80 contiguous nucleotides of SEQ ID NO: 9, whereas claims 7 and 8 recite a recombinant expression vector comprising the nucleic acid molecule and a host cell comprising the expression vector. However, other than SEQ ID NO: 9 that encodes SEQ ID NO: 10, the disclosure has not provided sufficient guidance and information regarding the structural and functional requirements commensurate in scope with what is encompassed by the instant claims. Due to lack of sufficient guidance and/or working examples, one of skilled in art would not know how to make and use the genus of nucleic acids in applications such as gene expression analysis or profiling, chromosomal mapping and genomic cloning, PCR, recombinant expression in a meaningful manner. Thus, the claims are broad.

At page 7 of Applicants' response filed on 08/17/2005, Applicants, citing case law, argue that a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. The Examiner agrees. However, in the instant case, due to lack of the relation of the function to structure of SEQ ID NO: 10 encoded by the nucleic acid sequence of SEQ ID NO: 9, one skilled in the art would not be able to make and use the genus of nucleic acids comprising at least 80 contiguous

bases of SEQ ID NO: 9, which has 2736 nucleotides and encodes a protein with 911 amino acids. Without disclosing portions of SEQ ID NO: 9 which are critical to the activity of the protein of SEQ ID NO: 10, an artisan would have to perform undue experimentation to find out those species that encoding a functional protein. Thus, different from the situations in cases cited by Applicants, an artisan would not be expected to make and use the claimed genus of nucleic acids, which comprises an enormous number of inoperative species, without undue experimentation.

Beginning at the bottom of page 7 of Applicants' response filed on 08/17/2005, Applicants, citing case law, that a specification "need describe the invention only in such detail as to enable a person skilled in the art in the most relevant art to make and use it." Examiner agrees. However, the instant specification fails to describe the claimed invention in such detail as to enable an artisan to make and use the claimed genus of nucleic acids for the reasons set forth above.

For the reasons above, the rejection of claims 1, 7, and 8 under 35 U.S.C. 112, first paragraph for scope of enablement is maintained.

Claim Rejections under 35 USC § 112, 1st paragraph, Written Description

The rejection of claims 1, 7, and 9 under 35 U. S. C. §112, 1st paragraph for written description is maintained.

At the middle of page 8 of Applicants' response filed on 08/17/2005, Applicants argue that the Action admitted that claims 1, 7, and 8 in fact do include a definitive structural feature of the claimed genus of nucleic acid molecules, specifically, that the nucleic acid molecule must include "a stretch of at least 80 consecutive nucleotides of SEQ ID NO: 9." Applicants further submit that this is all required of claims 1, 7, and 8 to meet the written description of 35 U.S.C. § 112, first paragraph.

Applicants' arguments have been fully considered but are not deemed to be persuasive because Applicants mischaracterize the Examiner's position. The Examiner never states that claims 1, 7, and 8 include a distinguishing feature. In fact, the previous Action clearly states that claim 1 is drawn to a genus of nucleic acid molecules comprising at least 80 contiguous nucleotides of SEQ ID NO: 9. Thus, it encompasses virtually any random sequence of any length as long as it has a stretch of at least 80 consecutive nucleotides of EQ ID NO: 9. The claim does not require that the nucleic acid molecules possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature.

Beginning at the bottom of page 8 of Applicants' response filed on 08/17/2005, Applicants summarize the description requirement by citing case law. Applicants argue that provision of a structure and formula—a nucleotide sequence—renders the application in compliance with 35 U.S.C. 112, first paragraph. Applicants submit that the nucleic acid sequences of the present invention are distinguished by structural

features—a chemical formula, i.e., the sequence itself. The skilled artisan would readily be able to distinguish the claimed nucleic acids from other materials on the basis of the specific structural description provided.

Applicants' argument has been fully considered, but is not deemed to be persuasive for the following reasons. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a recitation of partial structure: comprising at least 80 contiguous nucleotides of SEQ ID NO: 9. It is not a chemical formula because a chemical formula would accurately define the composition of a molecule. It does not represent a definitive structural feature because it says nothing about the biological activity, any particular conserved structure, or other disclosed distinguishing feature of the claimed genus and it says nothing about the relation of structure to function. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Only an isolated nucleic acid molecule comprising SEQ ID NO: 9, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph.

At the top page 10 of Applicants' response filed on 08/17/2005, Applicants criticize the Examiners' position and argue that structure or function is required, not structure and function. Applicants submit that as a precise definition of the structure and formula of the claimed genus sufficient to distinguish the genus from other materials is in fact provided in the present case, specifically the members of the genus comprises "a stretch of at least 80 consecutive nucleotides of EQ ID NO: 9 that is the same as SEQ ID NO: 9", the claimed invention is clearly in compliance with written description requirement under 35 U.S.C. §112, first paragraph.

Applicants' argument has been fully considered but is not deemed to be persuasive because "a stretch of at least 80 consecutive nucleotides of EQ ID NO: 9" does not represent a definitive structure or a chemical formula for the claimed genus, as noted above. SEQ ID NO: 9 consisting of 2736 nucleotides, there are enormous combinations of "at least 80 consecutive nucleotides of SEQ ID NO: 9", which cover different regions of SEQ ID NO: 9. The limitation "at least 80 consecutive nucleotides of EQ ID NO: 9" does not define a conserved structure. Consequently, there is no definitive function linked to such a limitation "at least 80 consecutive nucleotides of EQ ID NO: 9". Moreover, the claim uses an open language, "comprising", rendering the scope of the invention further broader. Accordingly, only an isolated nucleic acid molecule comprising SEQ ID NO: 9, but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph. It is also noted that a number of

factors, either alone or in combination, are considered to determine whether a specification is in complicance with the written description requirement.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00

pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (571) 272-0829. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

Ruixiang Li

Ruixiang Li, Ph.D.
Primary Examiner
October 6, 2005